

U.S. Patent Application No. 10/660,110  
Amendment dated February 10, 2009  
In Response to Office Action Mailed November 12, 2008

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-19. (Canceled).

20. (Currently Amended) A method for extending the dynamic range of a photodetector, the method comprising:

providing a photodetector configured in a first configuration comprising a first dynamic range having a first upper limit and a first lower limit;

performing a first measurement of the identifiable fluorescent signals with the photodetector at the first configuration such that the photodetector yields a first output signal representing the abundance of a first type of fluorescently labeled particles, and yields a second output signal representing the abundance of a second type of fluorescently labeled particles;

configuring the photodetector to a second configuration comprising a second dynamic range having a second upper limit that is greater than the first upper limit and a second lower limit that is greater than the first lower limit;

performing a second measurement of the identifiable fluorescent signals with the photodetector at the second configuration such that the photodetector yields a third output signal representing the abundance of the first type of fluorescently labeled particles, and yields a fourth

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output signal representing the abundance of the second type of fluorescently labeled particles, the first output signal exceeds the first upper limit, the third output signal is within the second dynamic range, the second output signal is within the first dynamic range, the fourth output signal is less than the second lower limit, and the particles of the first type of fluorescently labeled particles are more abundant in the sample than the particles of the second type of fluorescently labeled particles;

determining that the first output signal falls outside of the first dynamic range by determining that the first output signal is greater than the first upper limit; and

determining that the fourth output signal falls outside of the second dynamic range by determining that the fourth output signal is less than the second lower limit; and

combining the first measurement and the second measurement to determine a scaled representation of at least one of (1) the first output signal at the first configuration, wherein the scaled representation of the first output signal represents an output signal that was not within the first dynamic range of the photodetector in the first configuration, and (2) the fourth output signal at the second configuration, wherein the scaled representative of the fourth output signal represents an output signal that was not within the second dynamic range of the photodetector in the second configuration.

21-22. (Canceled)

23. (Previously Presented) The method of claim 20, wherein combining the first measurement and the second measurement comprises scaling the first output signal to a scale associated with the second configuration such that, based on the second configuration, the third

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output signal is measured and the first output signal is represented based on the scaling of the measured value from the third output signal at the second configuration.

24. (Previously Presented) The method of claim 23, wherein the scaling of the first output signal allows representation of both the second and first output signals when a dynamic range associated with the detector is limited and is not able to measure the first output signal at the first configuration.

25. (Previously Presented) The method of claim 24, wherein the photodetector is a charge-coupled device and the first configuration comprises an exposure duration  $T1$ .

26. (Previously Presented) The method of claim 25, wherein the second configuration comprises an exposure duration  $T2$ , wherein the exposure duration  $T2$  is shorter than the exposure duration  $T1$ .

27. (Previously Presented) The method of claim 26, wherein the combining comprises multiplying a value of the third output signal by a ratio  $T2/T1$  to determine the scaled representation of the first output signal at the first configuration.

28. (Previously Presented) The method of claim 24, wherein the photodetector is a charge multiplier and the first configuration comprises an operating voltage  $V1$ .

29. (Previously Presented) The method of claim 28, wherein the second configuration

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comprises an operating voltage V2, wherein the operating voltage V2 is lower than the operating voltage V1.

30. (Previously Presented) The method of claim 29, wherein the combining to determine comprises determining a scaled value N1' of the first output signal based on the third output signal and the relationship  $\log(N1') = m \log(V2/V1)$  where m represents a slope of a curve obtained by plotting the multiplier's gain versus the voltage in a log-log manner.

31. (Original) The method of claim 30, wherein the charge multiplier comprises a photomultiplier tube.

32. (Original) The method of claim 30, wherein the charge multiplier comprises a charge intensifier.

33. (Currently Amended) A method of extending the dynamic range of a photodetector that measures detectable fluorescent signals from a sample undergoing a biological analysis wherein the detectable fluorescent signals represent two or more components of the sample, the method comprising:

providing a photodetector configured in a first configuration comprising a first dynamic range having a first upper limit and a first lower limit;

performing a first measurement of the detectable fluorescent signals to obtain a first output signal and a second output signal from the photodetector operated at the first configuration such that the first output signal represents a first component of the detectable

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fluorescent signals, and the second output signal represents a second component of the detectable fluorescent signals;

configuring the photodetector in a second configuration comprising a second dynamic range having a second upper limit that is greater than the first upper limit and a second lower limit that is greater than the first lower limit;

performing a second measurement of the detectable fluorescent signals to obtain a third output signal and a fourth output signal from the photodetector operated at the second configuration such that the third output signal represents the first component of the detectable fluorescent signals and the fourth output signal represents the second component of the detectable fluorescent signals, wherein the first configuration is such that the first output signal of the first component of the detectable fluorescent signals falls outside the photodetector's first dynamic range; and

determining that the first output signal falls outside of the first dynamic range of the photodetector in the first configuration;

determining that the fourth output signal falls outside of the second dynamic range of the photodetector in the second configuration;

scaling separately the first output signal to a scale associated with the second configuration wherein the amount of scaling depends on the first and second configurations and the third output signal, wherein the separately scaled first output signal allows the generation of a scaled representation of the first output signal at the first configuration and the scaled representation of the first output signal represents an output signal that was not within the first dynamic range of the photodetector in the first configuration.

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34. (Previously Presented) The method of claim 33, wherein the first component of the detectable signals is stronger than the second component of the detectable signals.
35. (Canceled)
36. (Previously Presented) The method of claim 34, wherein scaling the first output signal allows representation of both the first and the second components when the dynamic range associated with the photodetector is limited and would not be able to measure the first component at the first configuration.
37. (Previously Presented) The method of claim 36, wherein the detector is a charge-coupled device and the first configuration comprises an exposure duration  $T1$ .
38. (Previously Presented) The method of claim 37, wherein the second configuration comprises an exposure duration  $T2$  selected to measure the second component of the detectable signals, wherein the duration of  $T1$  is longer than the duration of  $T2$ .
39. (Previously Presented) The method of claim 38, wherein the combining comprises multiplying a value of the third output signal by a ratio  $T2/T1$  to determine the scaled representation of the first output signal at the first configuration.
40. (Previously Presented) The method of claim 36, wherein the photodetector is a charge multiplier and the first configuration comprises an operating voltage  $V1$ .

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41. (Previously Presented) The method of claim 40, wherein the second configuration comprises an operating voltage  $V_2$  that is lower than the operating voltage  $V_1$ .

42. (Previously Presented) The method of claim 41, wherein the scaling of the first output signal comprises determining a scaled value  $N_1'$  of the first output signal based on the third output signal and the relationship  $\log(N_1') = m \log(V_2/V_1)$  where  $m$  represents a slope of a curve obtained by plotting the multiplier's gain versus the voltage in a log-log manner.

43. (Original) The method of claim 42, wherein the charge multiplier comprises a photomultiplier tube.

44. (Original) The method of claim 42, wherein the charge multiplier comprises a charge intensifier.

45. (Currently Amended) A method for extending the dynamic range of a photodetector, the method comprising:

providing a photodetector configured in a first configuration comprising a first dynamic range having a first upper limit and a first lower limit;

performing a first measurement of the identifiable fluorescent signals with the photodetector at the first configuration such that the photodetector yields a first output signal representing the abundance of a first type of fluorescently labeled particles, and yields a second output signal representing the abundance of a second type of fluorescently labeled particles;

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configuring the photodetector to a second configuration comprising a second dynamic range having a second upper limit that is less than the first upper limit and a second lower limit that is less than the first lower limit;

performing a second measurement of the identifiable fluorescent signals with the photodetector at the second configuration such that the photodetector yields a third output signal representing the abundance of the first type of fluorescently labeled particles, and yields a fourth output signal representing the abundance of the second type of particles, the first output signal is less than the first lower limit, the third output signal is within the second dynamic range, the second output signal is within the first dynamic range, the fourth output signal is greater than the second upper limit, and the particles of the second type of fluorescently labeled particles are more abundant in the sample than the particles of the first type of fluorescently labeled particles;

determining that the first output signal falls outside of the first dynamic range by determining that the first output signal is less than the first lower limit; ~~and~~

determining that the fourth output signal falls outside of the second dynamic range by determining that the fourth output signal is greater than the second upper limit; and

combining the first measurement and the second measurement to determine a scaled representation of at least one of (1) the first output signal at the first configuration, wherein the scaled representation of the first output signal represents an output signal that was not within the first dynamic range of the photodetector in the first configuration, and (2) the fourth output signal at the second configuration, wherein the scaled representative of the fourth output signal represents an output signal that was not within the second dynamic range of the photodetector in the second configuration.



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46. (Previously Presented) The method of claim 45, wherein combining the first measurement and the second measurement comprises scaling the first output signal to a scale associated with the second configuration such that, based on the second configuration, the third output signal is measured and the first output signal is represented based on the scaling of the measured value from the third output signal at the second configuration.

47. (Previously Presented) The method of claim 46, wherein the scaling of the first output signal allows representation of both the second and first output signals when a dynamic range associated with the photodetector is limited and is not able to measure the first output signal at the first configuration.

48. (Previously Presented) The method of claim 47, wherein the photodetector is a charge-coupled device and the first configuration comprises an exposure duration T1.

49. (Previously Presented) The method of claim 48, wherein the second configuration comprises an exposure duration T2, wherein the exposure duration T2 is longer than the exposure duration T1.

50. (Previously Presented) The method of claim 49, wherein the combining comprises multiplying a value of the third output signal by a ratio  $T2/T1$  to determine the scaled representation of the first output signal at the first configuration.

51. (Previously Presented) The method of claim 47, wherein the photodetector is a charge

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multiplier and the first configuration comprises an operating voltage V1.

52. (Previously Presented) The method of claim 51, wherein the second configuration comprises an operating voltage V2, wherein the operating voltage V2 is higher than the operating voltage V1.

53. (Previously Presented) The method of claim 52, wherein the combining to determine comprises determining a scaled value N1' of the first output signal based on the third output signal and the relationship  $\log(N1') = m \log(V2/V1)$  where m represents a slope of a curve obtained by plotting the multiplier's gain versus the voltage in a log-log manner.

54. (Previously Presented) The method of claim 53, wherein the charge multiplier comprises a photomultiplier tube.

55. (Previously Presented) The method of claim 53, wherein the charge multiplier comprises a charge intensifier.

56. (New) The method of claim 33, further comprising scaling the fourth output signal to a scale associated with the first configuration wherein the amount of scaling depends on the first and second configurations and the second output signal, wherein the scaled fourth output signal allows the generation of a scaled representation of the fourth output signal at the first configuration and the scaled representation of the fourth output signal represents an output signal that was not within the second dynamic range of the photodetector in the second configuration.

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57. (New) A method for extending the dynamic range of a photodetector, the method comprising:

providing a photodetector configured in a first configuration comprising a first dynamic range having a first upper limit and a first lower limit;

performing a first measurement of photoelectrons with the photodetector at the first configuration such that the photodetector yields a first output signal representing pixels that accumulate charge above a noise level and yields a second output signal representing pixels that do not accumulate charge above the noise level;

configuring the photodetector to a second configuration comprising a second dynamic range having a second upper limit that is greater than the first upper limit, and a second lower limit that is greater than the first lower limit;

performing a second measurement of photoelectrons with the photodetector at the second configuration such that the photodetector yields a third output signal representing pixels that accumulate charge above the noise level and above an anti-blooming threshold, and yields a fourth output signal representing pixels that accumulate charge above the noise level but not above the anti-blooming threshold, wherein the first output signal exceeds the first upper limit, the third output signal is within the second dynamic range, the second output signal is within the first dynamic range, and the fourth output signal is less than the second lower limit;

determining that the first output signal falls outside of the first dynamic range by determining that the first output signal is greater than the first upper limit;

determining that the fourth output signal falls outside of the second dynamic range by determining that the fourth output signal is less than the second lower limit; and

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combining the first measurement and the second measurement to extend the dynamic range of the photodetector.